REMARKS

Discussion of Amendments

Applicants have corrected inadvertent discrepancies in Fig. 2, 7-8, and 18. It is clear to those skilled in the art, based on the description of R_3, the R_2 on the left hand side of Fig. 2 must be R_3. There cannot be two R_2s. The formulas of compounds 11 and 12 in Fig. 7-8 have been corrected and are supported, for example, by the formulas of the same compounds shown in Fig. 3. The groups depicted on the left hand side of compounds 126 and A are OH groups, not the inadvertently shown MeO (Methoxy) groups, which were present in the precursors of these compounds.

Claim 39 has been amended by incorporating the limitation of claim 72. The proviso in claim 39 has been amended to remove an obvious discrepancy. The proviso should refer to Z and not W since arylalkylamino is only relevant for Z and not for W. Claim 40 has been amended by rewriting it as an independent claim and reciting that n is 1-15. Claim 67 has been amended to make it dependent upon claim 40. Claim 73 has been amended to make it dependent upon claim 39 and by more specifically defining "heterocyclyl portion" by replacing it with the term "arylheterocyclyl portion." The formula of the arylheterocyclyl portion in claim 73 has been redrawn to make it clearer that the left hand side ring of the formula must be aromatic and the right hand side (heterocyclic) ring may be aromatic or non-aromatic. Claims 85 and 117 have been amended by replacing "pharmacologically" with --pharmaceutically--. Claims 86, 91, 92, 118, and 122 have been amended to recite that the SH2 domain is part of a protein. Claim 123 has been amended to recite inhibition of proliferation of cells. New claims 124-136 have been added and are directed to embodiments of the invention. The amended and new claims are supported by the original specification and claims.

No new matter has been added.

The Present Invention

With the entry of the amendment, claims 39-49, 67-68, 73, 78, 85, 86, 91-93, 107, 113, 116-118, and 120-136 would be pending. Claims 86, 91, 92, 93, 107, 113, 118, 122-125, and 131-136 are directed to the use of the compounds of the presently claimed

invention. The previous Office Action indicated that use claims would be rejoined with composition claims. Accordingly, applicants respectfully request that the above use claims should be rejoined with the composition claims.

The Office Action

The Office Action sets forth the following grounds for rejection: (1) claim 123 is rejected under 35 U.S.C. § 101, for an alleged lack of utility, and under 35 U.S.C. § 112, first paragraph, for an alleged non-enablement; (2) claim 39 is rejected under the doctrine of obviousness-type double patenting as allegedly unpatentable over claim 1 or claim 11 of U.S. Patent No. 6,307,090; (3) claims 39-49, 67, 68, 72, 73, 78, 85, 116, 117, and 120-123 are rejected under 35 U.S.C. § 112, second paragraph, for an alleged indefiniteness; (4) claims 39, 40, 49, 72, 78, and 85 are rejected under 35 U.S.C. § 103(a), as allegedly anticipated by Al-Obeidi (USP 5,849,510); (5) claims 39, 40, 49, 67, and 78 are rejected under 35 U.S.C. § 102(e), as allegedly anticipated by Larsen (USP 6,410,585); (6) claims 39, 40, 49, 67, and 78 are rejected under 35 U.S.C. § 102(e), as allegedly anticipated by Horwell (USP 5,981,755); and (7) claim 39 is rejected under 35 U.S.C. § 102(e), as allegedly anticipated by Burke (USP 6,307,090), Hiyoshi (USP 5,824,862), Harding (USP 6,022,696), and Landry (USP 5,948,658).

Discussion of Rejections

a. Utility and Enablement

Claim 123 has been amended to remove the word "preventing." In view of the foregoing, the rejections under §§ 101 and 112, first paragraph, for the alleged lack of utility should be withdrawn.

Claim 123 also has been amended to recite cancer rather than disease, state or condition. This should remove the rejection based on the alleged non-enablement. The Office Action states that "on page 44, line 48+, it is asserted that addition of unidentified compounds to identified cells led the applicants to postulate that unidentified compounds of the invention have cell killing activity. However, given that the cells were unidentified, the compounds were unidentified and the results have not been disclosed, it is entirely possible that this particular result is in error." Applicants respectfully disagree. As set forth at page

44, lines 20+, the cell killing activity results are clearly set forth in Figure 17. It is clearly identified in Figure 17A that compounds 11, 12, 38, and 36 were tested. These compounds are covered by the presently claimed invention. It is clearly stated that MDA-453 cells are inhibited by the treatment with the tested inhibitors. Thus, the Office Action's conclusion above is clearly erroneous. The results discussed on page 45 clearly show those skilled in the art that the compound of the presently claimed invention inhibits the production of MAP kinase in MDA-453 cells that had been treated with heregulin. The Office Action has no basis to doubt the veracity of statements made by the inventors in the specification. Further, it is not required that a disease should be shown to be treated in a patient for enabling a treatment claim. The assays used by the present invention, the Biacore binding assay, the cell growth and proliferation, the MAP kinase inhibition assay are art-recognized assay methods and information obtained from these methods are applicable for enabling patent claims to treatment methods. As set forth at page 45, lines 25-27, applicants found excellent agreement between the data obtained from Biacore binding assay and ELISA assay.

The Office Action goes on to cite several references showing that inhibition of the farnesyl protein transferase leads to unpredictable results. The Office Action is misapplying the enablement requirement. The United States Patent and Trademark Office has in fact issued patents based on in vitro test data for cancer or even prophetic cell culture tests for the inhibition of farnesyl protein transferase. See, for example, U.S. Patents 6,743,786 and 6,740,661 (copies attached for the convenience of the Examiner). In view of the foregoing, claim 123 as presently amended should not be rejected for non-enablement. Claims 93, 107, and 133-136 also should not be rejected on this basis.

b. Obviousness-Type Double Patenting

As claim 39 has been amended, applicants believe that there is no obviousness-type double patenting over claim 1 or 11 of U.S. Patent 6,307,090. Claims 1 and 11 of the '090 patent do not suggest to those of ordinary skill in the art the subject matter of claim 39, either prior to or after the amendment. Particularly, the cited claims do not suggest to those of ordinary skill in the art group Z of the present claim. Group Y in cited claims 1 and 11 are merely a "secondary amino group". The corresponding part Z in the present claims is an arylalkylamino or arylheterocyclyl C_1-C_6 alkylamino. The term "secondary amino group"

does not suggest to those of ordinary skill in the art the presently recited Z groups. In view of the foregoing, the obviousness-type double patenting rejection should be removed.

c. Indefiniteness

Applicants respectfully traverse these rejections. The Office Action has queried the range of options for substituting aryloxycarbonyl with a keto group. Applicants respectfully submit that the range of options is clear to those skilled in the art. For example, the oxygen atom of the aryloxy group (the O attached to the ring) can be replaced with a keto group thereby providing an aryl diketo compound.

The Office Action contends that the phrase "the alkylamido group" in the last two lines of claim 39 lacks antecedent basis. Applicants respectfully submit that there is an inherent antecedent basis. Since phenylalanine has a phenyl ring with a CH_2CH followed by an amide group at the alpha carbon,, the term "alkylamido group" clearly identifies the intended group, for example, CH_2CH.

As regards claim 73, the presently amended claim should overcome the concern relating to the meaning of "heterocyclyl portion" of Z. Applicants have now more specifically described that the "arylheterocyclyl" portion of Z (in arylheterocyclyl C_1-C_6 alkylamino) is as shown by the formula. Further, the formula of the arylheterocyclyl portion has been redrawn. In accordance with the presently claimed invention, the ring on the left hand side (shown with three double bonds) must be aromatic; the fused ring structure containing F and G can be aromatic or non-aromatic. Accordingly, the part of the fused ring structure containing F and G is shown with dotted line.

In view of the amendments to claims 85 and 117, wherein "pharmacologically" has been replaced with --pharmaceutically--, the comments relating to these claims are no longer applicable.

Claim 122 has been amended to recite that the SH2 domain is part of a protein. Accordingly, the concern expressed with respect to claim 122 is no longer applicable.

In view of the amendments to claim 123, the comments relating to different embodiments of disease, state or condition are no longer applicable.

In view of all of the foregoing, the indefiniteness rejections should be withdrawn.

d. Anticipation

Applicants respectfully traverse the rejection of claims 39, 40, 49, 72, 78, and 85 with respect to Al-Obeidi. Al-Obeidi discloses at column 22, line 15+, a compound wherein the group at the right-hand side (CH_2-pyridyl) is not an arylheterocyclyl alkyl amino. The disclosed compound is merely a heterocyclylalkylamino. The claims require an additional aryl group. Accordingly, Al-Obeidi fails to anticipate the present claims.

The claims also are patentable over Larsen as well as Horwell. Since claim 39 has been amended to match the language of previous claim 72, which has not been rejected under Larsen or Horwell, claim 39 should be patentable over these references. In claim 40, n is 1-15. Larsen and Horwell recite n = 0. Claims 49, 67, and 78 are dependent upon claim 39 or 40. Accordingly, claims 39, 40, 49, 67, and 78 should be patentable.

As claim 39 is now amended (to match the language of claim 72), Burke should not be used to reject this claim. Further, applicants have discussed above the existence of antecedent basis for the term "alkylamido group." There is no ambiguity as to the meaning of the term "alkylamido group."

The rejections over Hiyoshi, Harding, and Landry of claim 39 should be removed because the claim has been amended to match the language of claim 72. The Office Action did not reject claim 72 over these references.

In view of the foregoing, the anticipation rejections should be removed. New claims 124-136 also should not be rejected on this basis since the cited references fail to disclose the invention recited in these claims.

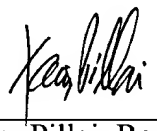
Request for a Corrected Official Filing Receipt

Applicants previously filed a Request for a Corrected Official Filing Receipt seeking a correction of the spelling error of one of the inventors' name, said error being not due to applicants' mistake. Applicants enclose a copy of the Request along with an indication of the requested change, and again, respectfully request that a Corrected Official Filing Receipt be issued.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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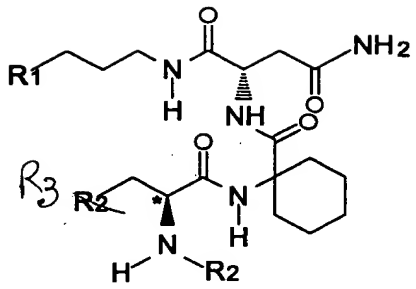
Date: June 25, 2004



General Structure
(*D, L and racemate claimed)

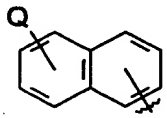
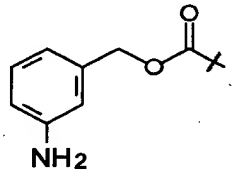
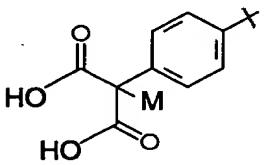
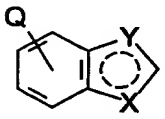
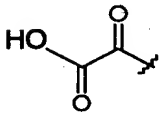
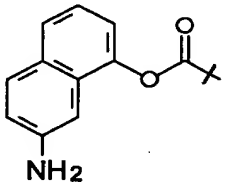
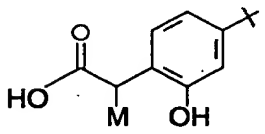
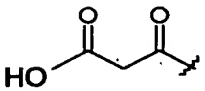
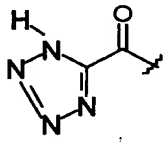
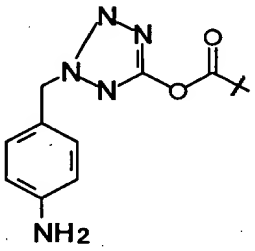
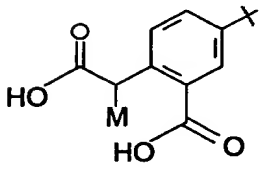
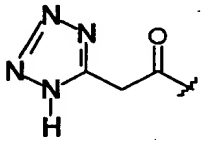
R_1	R_2	R_3
 1 and 2-substitued naphthyl	 	
 where Q=Me, short alkyl, halogen, hydroxy, alkyloxy, amino, acylamino	 	
		
	 	 where M= hydroxy, alkyloxy, halogen, keto, short alkyl
		

FIG. 2

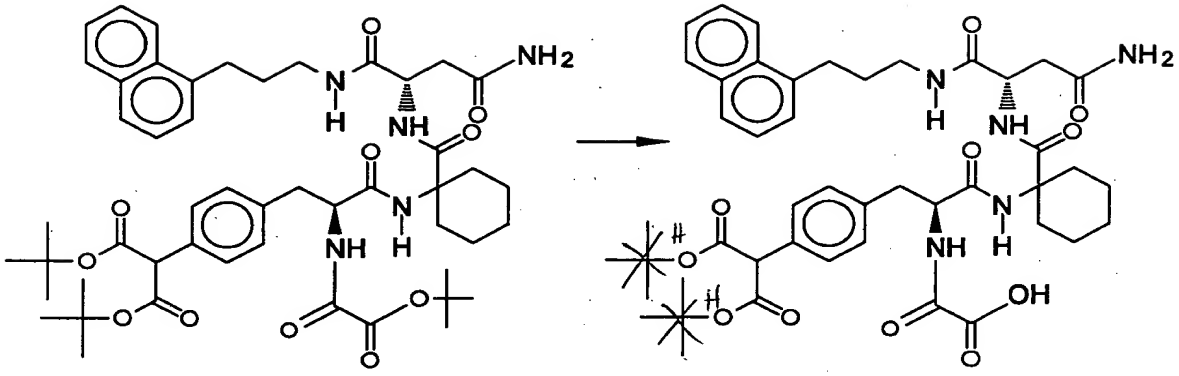


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FIG. 7

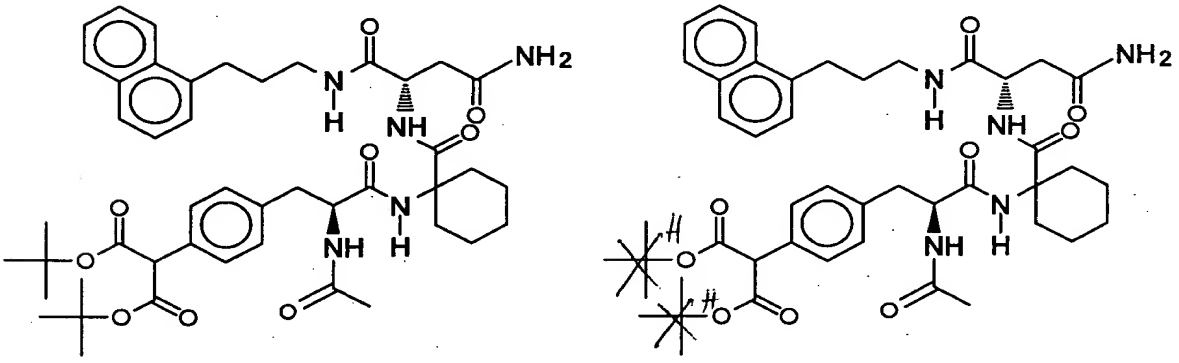

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FIG. 8

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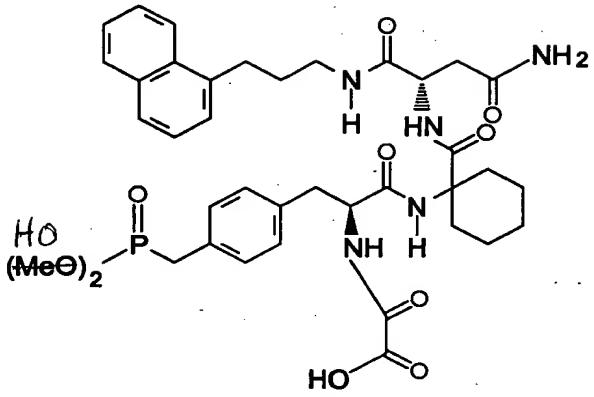
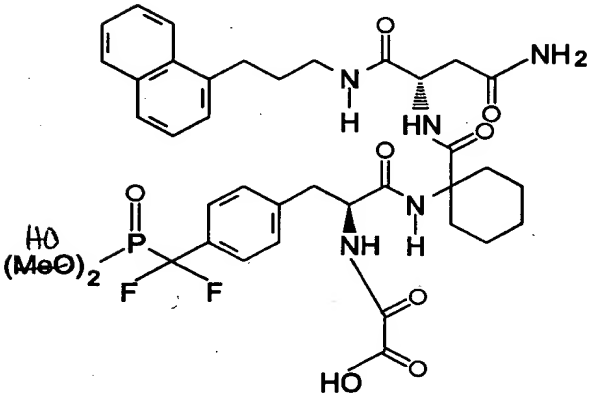
FIG. 18



Compd 126



Compd A